SYSTEMATIC REVIEW

The Effect of Neuroscience Education on Pain, Disability, Anxiety, and Stress in Chronic Musculoskeletal Pain

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ABSTRACT. Louw A, Diener I, Butler DS, Puentedura EJ. The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain. Arch Phys Med Rehabil 2011;92:2041-56.

Objective: To evaluate the evidence for the effectiveness of neuroscience education (NE) for pain, disability, anxiety, and stress in chronic musculoskeletal (MSK) pain.

Data Sources: Systematic searches were conducted on Biomed Central, BMJ.com, CINAHL, the Cochrane Library, NLM Central Gateway, OVID, ProQuest (Digital Dissertations), PsycInfo, PubMed/Medline, ScienceDirect, and Web of Science. Secondary searching (PEARLing) was undertaken, whereby reference lists of the selected articles were reviewed for additional references not identified in the primary search.

Study Selection: All experimental studies including randomized controlled trials (RCTs), nonrandomized clinical trials, and case series evaluating the effect of NE on pain, disability, anxiety, and stress for chronic MSK pain were considered for inclusion. Additional limitations: studies published in English, published within the last 10 years, and patients older than 18 years. No limitations were set on specific outcome measures of pain, disability, anxiety, and stress.

Data Extraction: Data were extracted using the participants, interventions, comparison, and outcomes (PICO) approach.

Data Synthesis: Methodological quality was assessed by 2 reviewers using the Critical Review Form–Quantitative Studies. This review includes 8 studies comprising 6 high-quality RCTs, 1 pseudo-RCT, and 1 comparative study involving 401 subjects. Most articles were of good quality, with no studies rated as poor or fair. Heterogeneity across the studies with respect to participants, interventions evaluated, and outcome measures used prevented meta-analyses. Narrative synthesis of results, based on effect size, established compelling evidence that NE may be effective in reducing pain ratings, increasing function, addressing catastrophization, and improving movement in chronic MSK pain.

Conclusions: For chronic MSK pain disorders, there is compelling evidence that an educational strategy addressing neurophysiology and neurobiology of pain can have a positive effect on pain, disability, catastrophization, and physical performance.

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PAIN IS A POWERFUL motivating force that guides treatment-seeking behaviors in patients.[1-3] Patient education has long been explored in the management of pain, anxiety, and stress associated with low back pain (LBP).[4-7] In the orthopedic domain, there are a number of studies on the effect of patient education on pain, with outcomes ranging from "excellent"[8] to "poor."[9,10] The study by Udermann et al[8] demonstrated that introduction of an individualized educational booklet on back biomechanics can result in decreased pain and frequency of LBP episodes in patients with chronic LBP (CLBP). In contrast to those findings, 2 systematic reviews[9,10] on the effect of individualized and/or group education for LBP and mechanical neck pain showed little efficacy for such education.

Most education programs for orthopedic patient populations have used anatomic and biomechanical models for addressing pain,[4,11-14] which not only have shown limited efficacy,[4,11,12,15,16] but may even have increased patient fears, anxiety, and stress, thus negatively impacting their outcomes.[11,17-19] Several educational strategies are advocated for patients with LBP, including biomechanical/back school type of education, evidence-based guideline education (ie, *The Back Book*[20]), cognitive behavioral therapy, and recently, neuroscience education (NE).

NE can be best described as an educational session or sessions describing the neurobiology and neurophysiology of pain, and pain processing by the nervous system. Instead of a

List of Abbreviations

BPPT	brachial plexus provocation test
CFS	chronic fatigue syndrome
CLBP	chronic low back pain
CONSORT	Consolidated Standards of Reporting Trials
LBP	low back pain
MSK	musculoskeletal
NE	neuroscience education
NPRS	numeric pain rating scale
PCI	Pain Coping Inventory
PCS	Pain Catastrophization Scale
PICO	participants, interventions, comparison, outcomes
PPT	pressure pain threshold
PSEQ	Pain Self-Efficacy Questionnaire
RCT	randomized controlled trial
RMDQ	Roland Morris Disability Questionnaire
SLR	straight leg raise
SOPA(R)	Survey of Pain Attitudes (Revised)
TSK	Tampa Scale of Kinesiophobia
VAS	visual analog scale
WAD	whiplash-associated disorders

Table 1: Inclusion Criteria Used in the Systematic Review

Criterion	Justification
English Language	Major journals in this area are published in this language.
1999–2010	Ten years captures the most recently used treatments in clinical practice. First such study to be published was by Moseley[27] in 2002.
Humans older than 18 years	This increased the homogeneity of participants between studies, and educational needs are different for infants, adolescents, and teenagers.[82,83]
MSK pain	This increased the homogeneity of conditions being managed with educational strategies incorporating NE.
Quantitative study design including RCTs, nonrandomized clinical trials, or case series	Study designs other than RCTs were included in this review because they provide complementary and relevant clinical detail to the current state of our knowledge and its limitations.[84,85] Single case studies were not included because of the low level of evidence they provide.
NE	Patient education is widely used to address pain, anxiety, and stress, but this review focused on educational strategies incorporating NE.
Outcomes: pain, disability, anxiety, and fear	The primary outcome measures chosen for this review were pain, disability, anxiety, and fear. No limitations were set on the measurement tool used to examine the effect of NE on pain, disability, anxiety, and fear.

traditional model of connecting tissue injury or nociception and pain, NE aims to describe how the nervous system, through peripheral nerve sensitization, central sensitization, synaptic activity, and brain processing, interprets information from the tissues and that neural activation, as either upregulation or downregulation, has the ability to modulate the pain experience. Patients are thus educated that the nervous system's processing of their injury, in conjunction with various psychosocial aspects, determines their pain experience and that pain is not always a true representation of the status of the tissues. By reconceptualizing their pain as the nervous system's interpretation of the threat of the injury, rather than an accurate measure of the degree of injury in their tissues, patients may be more inclined to move, exercise, and push into some discomfort. Depending on the timing of its administration, NE may be viewed as a preventive measure in acute pain situations and as a treatment/rehabilitation intervention in chronic pain situations.

Research into educational strategies for patients with CLBP shows an increased use of NE.[14,21-23] NE is a cognitive-based education intervention that aims to reduce pain and disability by helping patients gain an increased understanding of the biological processes underpinning their pain state.[24] NE differs from traditional education strategies such as back school and biomechanical models, by not focusing on anatomic or biomechanical models, but rather on neurophysiology, neurobiology, and the processing and representation of pain.[22,24,25] Patients are interested in knowing more about pain,[3] and it has been demonstrated that patients are capable of understanding the neurophysiology of pain, while professionals have underestimated patients' ability to understand the "complex" issues related to pain.[26]

Studies that used NE have been shown to decrease fear and positively change a patient's perception of their pain[21] and have an immediate effect on improvements in patients' attitudes about pain.[13] This education intervention also resulted in improvements in pain, cognition, and physical performance[14]; increased pain thresholds during physical tasks[23]; improved outcomes of therapeutic exercises[27]; and a significant reduction in widespread brain activity characteristic of a pain experience.[22] In 1 NE study,[27] results extended beyond the short-term and were maintained at 1-year follow-up.

Despite the proposed positive effects reported as a result of NE and the apparent increased use of NE, very little is known about the efficacy, content, and delivery methods of NE. Therefore, the objective of this systematic review was to source and critically evaluate NE. The results of this review could be used to make evidence-based recommendations regarding the utilization of NE for pain, disability, anxiety, and stress in chronic musculoskeletal (MSK) pain.

METHODS

Search Strategy

An electronic search was performed between February 2010 and July 2010, covering the last decade (1999–2010) from the following databases: Biomed Central, BMJ.com, CINAHL, the Cochrane Library, NLM Central Gateway, OVID, ProQuest (Digital Dissertations), PsycInfo, PubMed/Medline, ScienceDirect, and Web of Science. Each database has its own indexing terms and functions, and therefore different search strategies were developed for each database by the authors. The main search items were *neuroscience, neurobiology, neurophysiology, pain, pain education, pain science, education, stress,* and *anxiety.* In PubMed, medical subject headings (MeSH) terms were used where possible, with Boolean operators. The search strategies for remaining databases included synonyms of the main search items. Secondary searching (PEARLing) was undertaken, whereby reference lists of the selected articles were reviewed for additional references not identified in the primary search. The titles and abstracts of all the identified literature were screened by 1 primary reviewer using the inclusion criteria below. The full text of all potentially relevant articles was retrieved and screened by 2 reviewers using the same criteria, to determine the eligibility of the article for inclusion in the review.

Inclusion Criteria

All titles and abstracts were read to identify relevant articles. Articles were included in this systematic review if they met the inclusion criteria listed in table 1. Although outcome measures aimed at addressing MSK pain, disability, anxiety, and stress were included, no parameters were set on the exact measurement tools used to assess the effect of NE on pain, disability, anxiety, and stress, since a wide variety of outcome measures were used in the studies. When there was uncertainty regarding the eligibility of the article from the abstract, the full text

Table 2: Hierarchy of Evidence and Study Design, Based on the Australian National Health and Medical Research Council Hierarchy of Evidence*

Level	Definition	Studies
I	Evidence obtained from a systematic review of all relevant RCTs	
II	Evidence obtained from at least 1 properly designated RCT	Ryan et al,[24] Meeus et al,[25] Moseley,[14,21,27] Moseley et al[23]
III-1	Evidence obtained from well-designed pseudo-RCTs (alternate allocation or some other method)	Moseley[26]
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomized, cohort studies, case-control studies, or interrupted time series with a control group	
III-3	Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series without a parallel control group	Van Oosterwijck et al[41]
IV	Evidence obtained from case series, either posttest or pretest/posttest	

*Australian National Health and Medical Research Council.[87]

version of the article was retrieved and evaluated against the inclusion criteria. The full text versions of all articles that met the inclusion criteria were retrieved for quality assessment and data extraction (fig 1).

Quality Assessment

Critical appraisal of each included study was conducted by determining the following:

- *The level of evidence:* The level of evidence on the Australian National Health and Medical Research Council Hierarchy of Evidence (Australian National Health and Medical Research Council, 1999) provides a broad indication of bias based on study design (table 2). Studies higher on the hierarchy potentially contain less bias than those that are lower on the hierarchy.
- *The methodological quality:* The methodological quality of each study was assessed using the Critical Review Form–Quantitative Studies.[28] This tool can be used to appraise all types of quantitative studies ranging from randomized controlled trials (RCTs) to case series. Thus, all quantitative studies on NE for pain, disability, anxiety, and stress were included in this review and evaluated for quality using the same tool. This made the quality of results comparable between the different study designs.[29] Standardized guidelines on the interpretation and scoring of each item were used.[30] Items were scored as 1 (completely fulfills the criterion) or 0 (does not completely fulfill the criterion). The scores of the 16 closed-ended questions were tallied to provide an overall score of quality, where the maximum score of 16 indicated excellent quality.[31] Two researchers independently scored the studies and where disagreement occurred, consensus was achieved by discussion. Quality scores were arbitrarily divided into 5 categories: poor (score, $\leq$8), fair (score, 9–10), good (score, 11–12), very good (score, 13–14), and excellent (score, $\geq$15).[32] The Critical Review Form–Quantitative Studies[28] includes 17 of the 22 items that are contained in the Consolidated Standards of Reporting Trials (CONSORT) statement.[33,34] It does not include items 1 (study design stated in title or abstract); 8, 9, and 10 (randomization: sequence generation, allocation concealment, and implementation, respectively); or 19 (adverse events). The CONSORT statement was not designed to evaluate methodological quality.[33] However, in this review, it was documented whether these 5 CONSORT criteria were fulfilled by the RCTs. This step provides further methodological quality information.

Outcome Assessment

To determine the possible influence of NE on pain, disability, anxiety, and stress for chronic MSK pain, results were posted in narrative form, and outcomes were defined as "positive" (experimental group obtained a significantly greater improvement than the control group), "neutral" (there were no statistically significant differences between the groups), or "negative" (the control group obtained a significant greater improvement than the experimental group). An α of $P < .05$ was used to define a significant outcome measure. This method, used in previous systematic reviews, demonstrated 4 levels of scientific evidence on the quality and the outcome of the trials[35,36]:

1. *Strong evidence*: Multiple, relevant, high-quality RCTs with generally consistent outcomes.
2. *Moderate evidence*: One relevant, high-quality RCT AND 1 or more relevant, low-quality RCTs with generally consistent outcomes.
3. *Limited evidence*: One relevant, high-quality RCT OR multiple, relevant, low-quality RCTs with generally consistent outcomes.
4. *Inconclusive evidence*: Only 1 relevant, low-quality RCT; no relevant RCTs; or randomized trials with inconsistent outcomes.

A study was considered "relevant" when at least 1 of the outcome measures concerned pain or disability. For being "generally consistent," at least 75% of the trials that analyzed the same NE had to have the same result (positive, neutral, or negative).

Data Extraction

Data were extracted by the authors using the PICO (participants, interventions, comparison, outcomes) approach.[37]

- *Participants*: Diagnosis treated, age, sex, duration of the symptoms, type of referral source, and diagnostic criteria.
- *Interventions*: Type, intensity, duration, educational tools/props, in combination or stand-alone physical therapy.
- *Comparison*: To another treatment, no treatment, or "usual" treatment.
- *Outcomes*: Domains and tools used to measure the effects of the intervention. Outcomes chosen for this review included pain, disability, anxiety, and stress.

Data on the effectiveness of the NE were also extracted for each study. To determine the effect of the NE on each outcome measure, the mean and 95% confidence intervals for the between-group differences were calculated for RCTs and comparative studies, based on the results provided in each article.[38] Moreover, the mean changes between pretreatment and posttreatment (and 95% confidence intervals) were calculated for the RCTs and comparative studies. Pain reduction of more than 20%, irrespective of the measurement tool used, was considered clinically worthwhile.[39,40] It was expected that there would be heterogeneity in participants, interventions, comparisons, and outcomes. Therefore, the results of the studies were synthesized in a narrative format.

RESULTS

Search Strategy Yield

Initially, 15,382 hits were gained from databases and secondary searches. After review of the titles and abstracts, those articles that did not meet the inclusion criteria were removed. After reviewing 779 abstracts, the full text of 43 articles was reviewed. On further review, duplicates were removed, leaving 8 studies for the systematic review. This systematic review is based on 8 published studies.[14,21,23-27,41]

Critical Appraisal

Hierarchy of evidence. There were 6 RCTs,[14,21,23-25,27] 1 pseudo-RCT,[26] and 1 comparative study[41] (see table 2).

Methodological quality. There was 100% agreement in scoring between the researchers conducting the systematic review. Variation in methodological quality was noted (table 3), with scores ranging from 11 to 15 (mean, 13/16). Most articles were "good" in quality, 2 were "very good," and 2 were "excellent." No articles were rated as "poor" or "fair." Table 3 provides details regarding the criteria that were fulfilled on the Critical Review Form–Quantitative Studies.[28] It demonstrated that all studies provided adequate detail to allow for reproduction of their intervention (criterion 10). Six studies reported on the reliability of all their measurement tools (criterion 9), and 1 justified sample size (criterion 6). All studies were free from major biases (criterion 4), and 5 studies reported on the validity of all their measurement tools (criterion 8).

CONSORT criteria 1, 8, 9, 10, and 19. Table 3 also provides details regarding the fulfillment of the CONSORT criteria. Only about half of the studies complied with item 9 by reporting the method used to implement a random allocation sequence. Four studies[23-25,27] complied with item 10 by reporting who generated the allocation sequence, enrolled participants, and assigned participants to their groups. No studies complied with item 19 by reporting whether there were any adverse events in the intervention group.

Naming the intervention. NE is new and described as an educational intervention that aims to reduce pain and disability by explaining the biology of the pain experience to a patient.[22,24] In this review, it is noteworthy that the intervention of explaining the biological process behind a patient's pain state is described differently by the different authors:

- *Neurophysiology of pain* education[23,26,27]
- *Pain physiology* education[14,21,25]
- *Pain biology* education[24]
- *Pain neurophysiology* education[41]

Patient characteristics. In this review, NE was administered to 401 patients, of whom 63% were women (n=252). The average age of the patients ranged from 24±10 years[23] to 45.5±9.5 years,[24] with a mean age (calculated as the mean of the mean reported ages) of the patients receiving NE as 38.2 years. NE was presented to patients with LBP, chronic fatigue syndrome (CFS), widespread pain, and chronic whiplash-associated disorders (WAD). The LBP studies primarily focused on CLBP, with the average duration of symptoms ranging from 13.7±10.2 months[24] to 48±18 months,[26] with an average duration (calculated as a mean of the mean scores) of 31.2 months.

Content of NE. Details of the specific content of the educational sessions used in the studies are found in table 4. In summary, NE session contents included the following:

- Neurophysiology of pain[14,21,23-27,41]
- No reference to anatomic or pathoanatomic models[23,27]
- No discussion of emotional or behavioral aspects of pain[23]
- Nociception and nociceptive pathways[14,23,41]
- Neurons[14,41]
- Synapses[14,23,41]
- Action potential[14,41]
- Spinal inhibition and facilitation[14,23,41]
- Peripheral sensitization[14,23,41]
- Central sensitization[14,23,41]
- Plasticity of the nervous system[23,41]

It is also noteworthy that 4 studies[14,24,25,41] refer directly to the text, *Explain Pain,* as a source of the content of the NE used in their studies.

Educational Delivery Methods

Professionals performing NE. NE in the reviewed studies was performed by physical therapists. Only 1 study[25] failed to clearly identify the professional qualifications of the educator.

Duration and frequency of NE. The duration and frequency of the NE sessions were quite varied. Educational sessions lasted as long as 4 hours,[21] while more recent studies[25,41] reported sessions lasting 30 minutes. Educational sessions were also varied between single educational sessions[14,21,23-26] and multiple sessions.[21,27,41] The most common frequency between multiple educational sessions was 1 week apart.[21,27,41] Considering studies varied between single educational interventions and multiple interventions, total education time was also determined. On the high end, 1 study[27] spent 8 hours on NE, while the 2 studies[25,41] with the least amount of total time only spent 30 to 60 minutes on NE. The remainder of the studies averaged between 2.5 and 4 hours of total education time.

Educational format. The format in which the NE was delivered was primarily by means of one-on-one verbal communication.[14,21,23,25,27,41] Only 2 studies[21,26] used group sessions.

Educational tools. Details of the specific educational tools used during NE sessions are found in table 4. In summary, NE sessions are accompanied by the following:

- Prepared pictures[14,23-25,41]
- Examples[23,25,41]
- Metaphors[41]
- Hand drawings[14,24,26]
- Workbook with reading/question-answer assignments[23,27]
- Neurophysiology Pain Questionnaire[41]

Adjunct treatment to the NE. Several different research designs are included in this review. In all the studies, patients received various forms of other therapeutic interventions at various stages of the studies for various reasons. NE was thus

Table 3: Study Quality of the RCTs (n=8) Using the CONSORT Statement[33,34]

No.	Criterion–Critical Review Form	Moseley[27] 2002	Moseley[21] 2003	Moseley[26] 2003	Moseley[14] 2004	Moseley et al[23] 2004	Ryan et al[24] 2010	Meeus et al[25] 2010	Van Oosterwijck et al[41] 2011	Total
1	Purpose clearly stated	1	1	1	1	1	1	1	1	8
2	Literature review relevant	1	1	1	1	1	1	1	1	8
3	Study design appropriate to study design aims	1	1	1	1	1	1	1	1	8
4	No biases present	0	0	0	0	0	0	0	0	0
5	Sample description in detail	1	1	1	1	1	1	1	1	8
6	Sample size justified	0	0	0	0	0	0	1	0	1
7	Informed consent gained	0	1	0	1	0	1	1	0	4
8	Validity of outcome measures used	0	0	0	1	1	1	1	1	5
9	Reliability of outcome measures used	0	0	1	1	1	1	1	1	6
10	Intervention described in detail	1	1	1	1	1	1	1	1	8
11	Statistical reporting of results	1	1	1	1	1	1	1	1	8
12	Appropriate statistical analysis	1	1	1	1	1	1	1	1	8
13	Clinical importance reported	1	1	1	1	1	1	1	1	8
14	Appropriate conclusions	1	1	1	1	1	1	1	1	8
15	Clinical implications reported	1	1	1	1	1	1	1	1	8
16	Study limitations acknowledged	1	1	1	1	1	1	1	1	8
	TOTAL	11	12	12	14	12	15	15	13	
	Quality category*	Good	Good	Good	Very good	Good	Excellent	Excellent	Very good	
	Criterion–CONSORT statement†									
1	Study design stated in the title or abstract	X	X	X	X	√	√	√	X	
8	Randomization: sequence generation	√	X	X	X	√	√	X	X	
9	Randomization: allocation concealment	√	X	√	X	√	√	√	X	
10	Randomization: implementation	√	X	X	X	√	√	√	X	
19	Adverse events	X	X	X	X	X	X	X	X	

*Quality category: poor (score, ≤ 8); fair (score, 9–10); good (score, 11–12); very good (score, 13–14); and excellent (score, 15–16).[32]
†√ , criterion fulfilled; X, criterion not fulfilled.

preceded by, combined with, or followed by various therapeutic activities. The therapeutic activities that accompanied NE included the following:

- Manual therapy, including spinal mobilization and manipulation[27]
- Soft tissue treatment/massage[27]
- Neural tissue mobilization[27]
- Spinal stabilization exercises[21,24,27]
- Home exercises[27]
- Circuit training[24]

Table 4: Participants, Interventions and Outcomes in the Reviewed Studies

	Participants			Interventions		Outcomes	
Author	n	Sample Characteristics	Diagnostic Criteria	Treatment	Control	Outcome Instruments	Time of Assessment
Moseley[22] 2002	57	• LBP >2 months • Women: 59% • Age (y): EG, 43±7; CG, 38±7 • Duration of symptoms (mo): EG, 39±18; CG, 37±12	NA	Two physiotherapy sessions per week for 4 weeks Manual therapy including mobilization and manipulation, soft tissue massage, muscle and neural mobilization techniques, but no electrophysical modalities Specific trunk stabilization program Maintain home exercises indefinitely One-hour educational session once a week for 4 weeks One-on-one education format by an independent therapist Content: neurophysiology of pain with no reference to lumbar spine, accompanied by workbook with 1 page of revision material and 3 comprehensive exercises per day for 10 days	Ongoing medical care as advised by their general practitioner No attendance of physiotherapy	• NRS: meaningful difference set at 2 points • RMDQ: meaningful difference set at 4 points • NNT	Baseline; 1 month after intervention and 1 year after intervention
Moseley[21] 2003	276 288	Patients: • Women: trained group, 61%; untrained group, 68% • Age (y): trained group, 43±9; untrained group, 37±17. • Duration of pain (y): trained group, 4±1.5; untrained group, 3±1 Professionals: • 21 exercise therapists • 30 medical practitioners • 36 nurses • 44 occupational therapists • 44 psychologists • 57 physiotherapists • 28 rehabilitation counselors	NA	Patients: Direct lecture from a specifically trained physiotherapist Hand-drawn images Neurophysiology of pain Professionals: Seminar on neurophysiology of pain–3 hours in AV format provided by a physiotherapist	None	• Neurophysiology of pain questionnaire	Trained group: Immediately after the educational session Untrained group: Questionnaire before and after the educational session
Moseley[26] 2003	41	• LBP >3 months • Women: EG, 67%; CG, 60% • Age (y): EG, 40±7; CG, 42±7 • Duration of symptoms (mo): EG, 33±11; CG, 30±14	NA	Individual 4 × 1-hour educational session on the physiology of pain and injury by a physiotherapist Additionally received 2 physiotherapy sessions per week for 4 weeks focusing on spinal stabilization exercises	Group session involved a single 4-hour session with a group of 7–10 patients provided by a physiotherapist Physiology of pain and injury Additionally received 2 physiotherapy sessions per week for 4 weeks focusing on spinal stabilization exercises	• NRS • RMDQ • NNT	Baseline; 1 month after "ongoing medical treatment" and 1 and 2 months after educational and physiotherapy sessions

Table 4 (Cont'd): Participants, Interventions and Outcomes in the Reviewed Studies

	Participants			Interventions		Outcomes	
Author	n	Sample Characteristics	Diagnostic Criteria	Treatment	Control	Outcome Instruments	Time of Assessment
Moseley[14] 2004	121	• LBP >4 months. • Women: EG, 50%; CG, 65%. • Age (y): EG, 36±6; CG, 35±7	NA	Single one-on-one educational session by a physiotherapist Physiology of pain and nociception - The neuron: receptor, axon, terminal - The synapse: neurotransmitters, chemically driven ion channel, postsynaptic membrane potential, action potential - Spinal and descending inhibition and facilitation - Peripheral sensitization - Central sensitization: potentiation of the postsynaptic membrane, altered genetic expression, and receptor field growth Lectures accompanied by hand drawings and prepared pictures with interactive commentary Sessions lasted approximately 3 hours	Single one-on-one educational session by a physiotherapist: Anatomy and physiology of the lumbar spine - The intervertebral disk: structure and physiology and the effect of aging - Vertebral canal and intervertebral foramen: thecal sac, spinal nerve root, ligamentum flavum - The facet joint: anatomy and biomechanics - The muscles: anatomy, physiology, antagonist and synergistic roles - Spinal biomechanics: curvatures, posture, and ergonomics Lectures accompanied by hand drawings and prepared pictures with interactive commentary Sessions lasted approximately 3 hours.	• Brief SOPA(R) • PCS • SLR (inclinometer) • Forward bending test (tape measure–longest finger to floor in flexed position)	Baseline data Preeducation and immediate posteducation
Moseley et al[23] 2004	58	• LBP >6 months • Age (y): EG, 24±10; CG, 45± 6 • Duration of pain (mo): EG, 18±11; CG, 20±11	NA	Education session by a physiotherapist in one-to-one seminar format: - Session lasted 3 hours; diagrams and hypothetical examples used as teaching tools - At conclusion: Workbook with 10 sections; patients asked to read 1 section per day and answer 3 questions on each session Neurophysiology Education: No specific application was made to the lower back, or to emotional and behavioral patterns commonly associated with chronic pain such as catastrophic thought processes or fear avoidance. *The Nervous System* Presentation of the basic structure of the nervous system, with a focus on the components of the nociception/pain pathways. This section included an outline of the functional significance of each component. *Synapses* Presentation of how nerves "talk to each other," including the concept of "chemicals" (neurotransmitters), postsynaptic receptors, and a conceptual "volume knob" (postsynaptic excitation and inhibition), with a special focus on the "danger messenger nerve" (second-order nociceptive neuron) *Plasticity of the Nervous System* The adaptability of the nervous system including the following: afferent and efferent pathways; the variable state of neural structures including normal state, peripheral, and central sensitization; receptor synthesis; axonal sprouting; the neural response to inactivity; and movement control	Education session by a physiotherapist in one-to-one seminar format: - Session lasted 3 hours; diagrams and hypothetical examples used as teaching tools - At conclusion: Workbook with 10 sections; patients asked to read 1 section per day and answer 3 questions on each session Back Education: Anatomy and physiology of the bones and joints of the lumbar spine; the intervertebral disk; the trunk and back muscles; normal spinal curves; posture and movements, including analysis of postures and activities according to intradiskal pressures and joint forces; lifting techniques and lifting loads; lifting aids and ergonomic advice; principles of stretching; and strength, endurance, and fitness training. It did not include information about the nervous system, except for outlining the location and course of the spinal cord and the spinal nerve roots. It was similar to education material that has been researched elsewhere and the education components of back schools and functional restoration programs.	• RMDQ • Brief SOPA(R) • PCS • SLR (inclinometer) • Forward bending range (distance from longest finger to floor) • Abdominal draw-in task	Pretreatment; 3 weeks

Table 4 (Cont'd): Participants, Interventions and Outcomes in the Reviewed Studies

	Participants			Interventions		Outcomes	
Author	n	Sample Characteristics	Diagnostic Criteria	Treatment	Control	Outcome Instruments	Time of Assessment
Ryan et al[24] 2010	38	• LBP >3 months Education group: • n=18 • 11 women • Age (y): 45.5±9.5 • Duration of pain (mo): 13.7±10.2 Education and exercise group: • n=20 • 14 women • Age (y): 45.2±11.9 • Duration of pain (mo): 7.6±7	NA	Pain Biology Only: 2.5-hour pain biology education session Cognitive behavioral intervention focused on reshaping participants' beliefs and attitudes about their back pain, attempting to decrease fear avoidance and harm beliefs, increase self-efficacy, and decrease avoidance behavior The biology of pain Verbal communication, prepared diagrams, and freehand drawings Additionally, all participants received *The Back Book*.	Pain Biology and Exercise: 2.5-hour pain biology education session Cognitive behavioral intervention focused on reshaping participants' beliefs and attitudes about their back pain, attempting to decrease fear avoidance and harm beliefs, increase self-efficacy, and decrease avoidance behavior The biology of pain Verbal communication, prepared diagrams, and freehand drawings Additionally, all participants received *The Back Book*. Exercise Component: "Back to Fitness exercise classes"; 6 classes, 1 a week for 6 weeks. The classes involved circuit-based, graded, aerobic exercise with some core stability exercises. The classes involved a warm-up phase (10min), an aerobic phase (20–30min), and a warm-down phase (10–15min). The aerobic phase involved circuit-based exercise. For most exercises there was an easy, moderate, and hard version, and the participant could choose which version to perform.	• RMDQ • NRS • Repeated sit-to-stand test • The 50-foot walk test • 5-minute walk test • TSK-13 • PSEQ • Step count (activPAL activity monitor[c])	Pretreatment and 8 weeks later; 3 months later
Meeus et al[25] 2010	46	• CFS and widespread pain • Women: EG, 22; CG, 18 • Age (y): EG, 38.3±10.6; CG, 42.3±10.2	1994 Centers for Disease Control and Prevention criteria for CFS[86]	Pain Physiology: One 30-minute interactive session Physiology of the nervous system in general and of the pain system in particular The theoretic information was illustrated with pictures and examples. The objective of the education was to teach patients the function, mechanisms, and modulation of (chronic) pain, and so forth.	Pacing and Self-Management: One 30-minute interactive session Pacing and self-management education was provided to all participants in the control group. Pacing is a strategy in which patients are encouraged to achieve an appropriate balance between activity and rest in order to avoid exacerbation and to set realistic goals for increasing activity. Following this energy management strategy, patients should avoid activities at an intensity that exacerbates symptoms, or they should intersperse activities with periods of rest.	• Neurophysiology of Pain Test • PCS • PCI • TSK • Pain threshold assessment (Fisher algometer[b])	Pretreatment and immediately posttreatment

Table 4 (Cont'd): Participants, Interventions and Outcomes in the Reviewed Studies

	Participants			Interventions		Outcomes	
Author	n	Sample Characteristics	Diagnostic Criteria	Treatment	Control	Outcome Instruments	Time of Assessment
Van Oosterwijck et al[41] 2011	6	• WAD grade I–II • 5 women, 1 man • Mean age (y): 35.6 • Mean duration of symptoms (mo): 50.3	WAD I-II according to Quebec Task Force on Whiplash-Associated Disorders	Two educational sessions and a leaflet on the neurophysiology of pain: One-on-one education session on neurophysiology of pain lasting 30 minutes; physiotherapist delivered the education session. Content and pictures based on the *Explain Pain* text; physiology of the nervous system in general and of the pain system in particular; pictures, examples, and metaphors were used. Topics addressed during the educational sessions included the characteristics of acute vs chronic pain; the purpose of acute pain; how acute pain originates in the nervous system (nociceptors, ion gates, neurons, action potential, nociception, peripheral sensitization, synapses, synaptic gap, inhibitory/excitatory chemicals, spinal cord, descending/ascending pain pathways, brain role, pain memory, and pain perception); how pain becomes chronic (plasticity of the nervous system, modulation, modification, central sensitization, pain neuromatrix theory); and potential sustaining factors of central sensitization such as emotions, stress, pain cognitions, and pain behavior. Educational session in line with the content of the Neurophysiology of Pain Test in such a way that after having received the education, patients should be able to answer all questions of the test correctly. The educational information was presented verbally (explanation by the therapist) and visually (summaries, pictures, and diagrams on computer and paper). Patients also received an information leaflet about the neurophysiology of pain and were asked to read it carefully at home. During the second session, the therapist answered and explained additional questions that arose after reading the information leaflet.	None	Primary outcome measures: • Neck Disability Index • PPT (Fisher algometer) Secondary outcomes: • WAD symptom list • PCS • PCI • TSK • Neck extension test • VAS • BPPT	A-B-C design: Period A, assessment before intervention (2–3wk); Period B, intervention (1wk) Period C, postintervention assessment (3wk) Total time, 7 weeks

Abbreviations: CG, control group; EG, experimental group; NA, not applicable; NNT, numbers needed to treat; NRS, numeric rating scale.

Table 5: Efficacy of NE on Pain, Disability, Anxiety, and Stress for MSK Conditions

Outcome	Moseley[21] 2003	Moseley[27] 2002	Ryan et al[24] 2010	Van Oosterwijck et al[41] 2011	Meeus et al[25] 2010	Moseley[26] 2003	Moseley et al[23] 2004	Moseley 2004[14]
Decrease pain ratings	+	+	+	+				
Increase knowledge of pain					+	+		
Increase pain tolerance				+	N			
Alter self-report whiplash symptoms				N				
Improve function and disability	+	+	N	+			+	
Decrease fear of reinjury			N	+	N			
Decreased pain catastrophization				N	+		+	+
Develop strategies to cope with pain				+	N			
Develop healthy attitudes regarding pain			N				+	+
Improve physical movement and performance			N	+			+	+

NOTE. + = positive (experimental group obtained a significantly greater improvement than the control group); N = neutral (there were no statistically significant differences between the groups).
Abbreviation: ●●●.

- Aerobic exercise[24]
- None (NE only)[14,23,25,26,41]

Use of Control Groups

Several different comparisons were made to groups receiving NE. Control interventions varied in the studies and included NE sessions compared with the following:

- Ongoing medical care[27]
- Not attending physical therapy[27]
- Health care professional knowledge of pain[26]
- Group session of NE[21]
- Anatomy and physiology of the lumbar spine[14,23,24]
- *The Back Book*[24]
- Exercise and NE combination[24]
- Pacing and self-management program[25]
- None[41]

Outcome Measures

There was great variability in outcome measurements across the studies in terms of the number and type of outcome measures used and the number of occasions they were used (see table 4). Researchers and clinicians using NE were interested in determining whether NE affected issues related to pain, disability, psychological issues associated with pain, and movement. A review of the outcome measures used in the studies revealed that most of the outcome measures fit into 1 of 4 categories:

1. Outcomes directly measuring issues related to pain
   - Pain ratings (numeric pain rating scale [NPRS] and visual analog scale [VAS])[21,24,27,41]
   - Pain knowledge (Neurophysiology of Pain Test)[25,26]
   - Pressure pain thresholds (PPTs)[25,41]
   - Self-report symptoms (WAD symptom list)[41]
2. Outcomes related to function and disability
   - Roland Morris Disability Questionnaire (RMDQ)[21,23,24,27]
   - Neck Disability Index[41]
3. Outcomes related to psychosocial issues
   - Tampa Scale of Kinesiophobia (TSK)[24,25,41]
   - Pain Catastrophization Scale (PCS)[14,23,25,41]
   - Pain Coping Inventory (PCI)[25,41]
   - Survey of Pain Attitudes (Revised) (SOPA[R])[14,23]
   - Pain Self-Efficacy Questionnaire (PSEQ)[24]
4. Movement
   - Neurodynamic tests: Straight leg raise (SLR) and brachial plexus provocation test (BPPT)[14,23,41]
   - Trunk forward flexion and neck extension[14,23,41]
   - Abdominal draw-in maneuver[23]
   - Endurance: Sit-to-stand, 50-foot walk test, 5-minute walk test, and step count[24]

Measurement periods were variable, ranging from immediate effect of NE[14,25,26,41] to 1-year follow-up,[21,27] but several studies also reported intermediate effects of NE.

Effectiveness of NE Data gained from the RCTs could not be pooled because of the heterogeneity of the outcome measures and comparison groups. Results are thus reported in narrative form and summarized in table 5.

NE addressing pain. Six of the 8 studies in this review examined the effectiveness of NE addressing issues associated with pain.[21,24-27,41] Methodological quality of the 6 studies addressing pain ranged from 11 (good) to 15 (excellent), with a mean score of 13.

- An NE session for patients with CLBP by itself produces a more favorable immediate effect on decreasing pain ratings (range, 0-100) (39.3±26.2 to 8.4±7.5) than a program combining NE and an exercise program (28.1±20.4 to 23.9±23.3) ($P<.025$), but loses its superior efficacy at 3-month follow-up.[24]
- NE for patients with CLBP decreased pain in both short-term (1mo) and long-term (1y) interventions ($P<.01$), compared with patients receiving ongoing medical care

without physical therapy.[27] The mean improvement of the NE session was 1.5 points on the NPRS.

- NE sessions for patients with CLBP delivered as single one-on-one sessions or as group sessions decreased pain significantly ($P<.05$), yet individual one-on-one educational sessions were associated with a more favorable outcome, compared with the group educational sessions ($P=.004$).[21] The average reduction in pain was 3.1 (1.8–4.2) for the individual education group versus 2.7 (1.6–3.9) in the group education session.
- After an NE session, patients with chronic WAD had a significant reduction in pain (VAS) during a neck extension test without fixation ($P=.04$) and with fixation ($P=.04$).[41] Perceived pain on the VAS was decreased 43.5% for the test without fixation and 59.2% with fixation.
- In patients with CFS, a 30-minute NE session is able to increase their knowledge of pain, compared with a program focused on pacing and self-management ($P<.001$).[25]
- A single NE session will increase the knowledge of pain in patients with CLBP.[26]
- NE did not improve PPT in patients with CFS,[25] while PPT was significantly increased (decreased sensitivity of the nervous system) in patients with chronic WAD (trapezius, $P=.03$; calf, $P=.04$).[41]
- Of all the self-report WAD symptoms on the WAD symptoms list (photophobia, neck mobility, and sweating), NE showed only a significant effect on decreasing photophobia ($P=.04$).[41]

NE addressing function and disability. Five of the 8 studies in this review examined the effectiveness of NE addressing issues associated with function and disability.[21,23,24,27,41] Methodological quality of the 5 studies addressing pain ranged from 11 (good) to 15 (excellent), with a mean score of 12.6.

- NE sessions for patients with CLBP delivered as single one-on-one sessions or as group sessions decrease disability (RMDQ) significantly ($P<.05$; average decrease 5.5 points), yet individual one-on-one educational sessions were associated with a more favorable outcome, compared with the group educational sessions ($P=.004$).[21] The change in RMDQ in this study was clinically meaningful and comparable to studies showing manipulation (3 RMDQ points)[42] and exercise (2.9 RMDQ points)[43] effects on changing disability.
- An NE session for patients with CLBP alters disability as measured by RMDQ ($P=.02$), but because of effect size (<2 points on the RMDQ) was clinically insignificant.
- NE for patients with CLBP decreased perceived disability in both the short-term (1mo) and long-term (1y) ($P<.01$), compared with patients receiving ongoing medical care without physical therapy.[27] The mean improvement on the RMDQ was 3.9 points for the experimental group, which is clinically significant.[27]
- NE reduced perceived disability in patients with CLBP, but failed to reach significance ($P=.127$). The immediate effect leveled off at 3-month follow-up.
- In measuring perceived disability from whiplash, Van Oosterwijck et al[41] showed that NE was able to decrease perceived disability ($P=.046$), which was reduced from 28.26% to 22.72%. This reduction is comparable to the disability decrease achieved by Moseley.[27]

Outcome related to psychosocial issues. *Tampa Scale of Kinesiophobia.* Three studies[24,25,41] used the TSK as an outcome measure to assess fear of (re)injury resulting from movement.

- A single NE session for patients with chronic WAD decreased fear of (re)injury ($P=.03$).[41]
- An NE program alone compared with an NE and exercise program failed to show any significant difference in pain-related fear as measured by the TSK ($P>.05$).[24]
- In a study[25] of patients with CFS, an NE session failed to show a significant difference in fear of (re)injury compared with a pacing and self-management program ($P>.05$).

Pain Catastrophization Scale. Four studies[14,23,25,41] used the PCS as an outcome measure to assess pain catastrophization.

- Meeus et al[25] evaluated the effect of NE compared with pacing and self-management for patients with CFS and found that NE changed 1 of the PCS factors (ruminating) by a statistically significant difference compared with the control group ($P<.05$).
- A single NE session for patients with chronic WAD showed no effect on pain catastrophization ($P>.05$).[41]
- An RCT[23] of patients with CLBP comparing NE to a back education program showed a statistical significant effect in decreasing pain catastrophization ($P<.001$).
- NE has been shown to decrease pain catastrophization ($P<.001$), which was correlated to increased SLR and forward bending.[14]

Pain Coping Inventory. Two studies[25,41] used the PCI as an outcome measure to assess cognitive and behavioral pain-coping strategies.

- In a study evaluating the effect of NE on patients with chronic WAD, NE changed passive coping strategies ($P=.03$), but not in the other PCI categories of retreating and worrying.
- Meeus[25] evaluated the effect of NE compared with pacing and self-management for patients with CFS and found that NE failed to produce a significant change in PCI ($P>.05$).[25]

Pain attitudes. Two studies[14,23] used the SOPA(R) as an outcome measure to assess attitudes and beliefs regarding pain.

- In an RCT comparing NE to back education, the NE session provided a significant change in patient attitudes and beliefs regarding pain, compared with the back education group ($P<.001$). Patients who received NE were less likely to seek care from others when they experienced pain; more likely to believe that they could control their pain; more likely to believe pain is affected by emotional distress; and less likely to believe pain is caused by tissue injury.[23]
- The study by Moseley[14] showed that an NE session altered 2 SOPA(R) factors significantly ($P<.05$)—harm and disability—which in turn were associated with increased physical performance.

Pain Self-Efficacy Questionnaire. Only 1 study[24] used the PSEQ as an outcome measure to determine individuals' beliefs regarding their ability to carry out activities and function despite their pain.

- In a study[24] comparing NE to a NE and exercise session, no statistically significant changes were found between the groups ($P>.05$).

NE addressing physical movement. Four[14,23,24,41] of the 8 studies in this review examined the effectiveness of NE in addressing issues associated with physical movement. Methodological quality of the 4 studies addressing physical movement ranged from 12 (good) to 15 (excellent), with a mean score of 13.5.

- *Neurodynamic tests:* NE compared with back education causes an immediate increase in SLR range of motion ($P<.01$)[14,23] including taking into consideration measurement error,[44] and decreased pain perception during a BPPT in patients with chronic WAD.[41]
- *Spine movements:* NE compared with back education causes an immediate increase in trunk forward flexion in patients with CLBP ($P<.01$),[14,23] and decreased pain perception during neck extension movements in patients with chronic WAD.[41]
- *Motor control:* NE compared with back education resulted in no statistical difference between the groups ($P>.05$).[23]
- *Physical performance:* NE compared with an NE and exercise program did not show a statistically significant difference ($P>.05$).[24]

DISCUSSION

Utilization of NE is increasing.[14,21-23,45,46] This is the first systematic review of NE for pain, disability, anxiety, and stress in patients with MSK pain. Although this review comprised a rather heterogeneous sample of studies using NE, the results indicate compelling evidence for the use of NE in decreasing pain ratings, increasing physical performance, decreasing perceived disability, and decreasing catastrophization in patients with chronic MSK pain.

NE focuses on a detailed description of the biology and physiology of the nervous system and brain's processing of pain and nociceptive input.[23,41] This approach is in direct contrast to prevailing biomedical models, which focus on tissues and tissue injury.[47-49] Orthopedic-based professions such as orthopedic surgeons and physical therapists commonly use anatomy- and pathoanatomy-based models to explain pain to their patients.[47-50] Not only have these models shown limited efficacy in decreasing pain and disability, but they may increase fear in patients, which in turn, may increase their pain.[51,52]

Although NE features an anatomic component (anatomy of the nervous system), it deemphasizes tissue injury (ie, disk or joint),[23,27] rather using the anatomy to describe pathways to process nociceptive input.[23,41] A key message that NE tries to impart to the patient is the clear difference between "nociception" and "pain." Patients are taught that the nervous system has the ability to increase or decrease its sensitivity (neuroplasticity) to help them cope with persistent pain.[23,41] Considering that other educational models use similar education delivery methods as NE, it could be argued that the content of NE may be the key element in its efficacy compared with the more traditional models of explaining pain to patients.[13,14,22,23,27]

The results indicate that one-on-one education was used the most[14,23-25,41] and is superior with respect to outcomes, when compared with group sessions.[26] Considering the individualistic and complex processing of pain, it should not be surprising that one-on-one educational sessions produced superior results.[13,26] Various brain pathways process nociception, and these pathways are influenced by personal experiences, thoughts, feelings, and emotions, thus creating an individual neural signature of the event.[13,53]

Although this review failed to identify the optimal duration and frequency of NE sessions, it is noteworthy that the 3 most recently published studies used considerably less education delivery time.[24,25,41] This reduction in time could be the result of an increased proficiency in applying NE, and also a potential means to develop an NE session that could be clinically useful,[25] potentially alleviating issues of time constraints in clinical practice.[54-56] This trend may allow clinicians to not only provide NE in as little as 30 to 45 minutes, but to also combine it with other physical treatments. The combination of NE and exercise[24,27,45] is in line with best-evidence guidelines for managing patients with chronic pain.[57-59] Physical therapists provided all the NE in this review.[14,21,23,25,27,41] Physical therapists' knowledge of neurophysiology and a movement-based approach may indicate a unique role for physical therapists in managing patients with chronic pain.

Educational sessions were also accompanied by various teaching tools, including hand-drawn images, prepared pictures, and workbooks.[14,23-25,41] The use of booklets concurs with patient education studies highlighting booklets as valuable tools in aiding information retention compared with verbal communication only.[60-62] In 2 of the NE studies,[23,27] patients were also asked to complete daily tasks. Patient tasks would likely aid in the development of much-needed deep learning processes, since the patient is active compared with a more passive education endeavor.[63-67]

Although various definitions for pain are provided in the scientific literature,[13,53] patients often see pain as a measure of the health of their tissues.[51,52] Pain is complex, and recent authors have highlighted that pain could possibly be a better measure of potential threat, rather than true tissue health.[13,22,68,69] The larger the threat, the more pain is perceived.[22] Patients' pain perception attributable to tissue health is yet another example of an anatomy and pathoanatomy model driving pain. Considering that NE purposefully deemphasizes tissue injury, focuses on the processing of nociception, and aims to increase the patient's awareness that nociception and pain are not correlated, it could be seen as a possible mechanism to decrease the threat, thus dampening the pain perception in the patient.[22,58]

Several studies[70-73] have shown that patients with higher pain ratings have increased disability. Because patients view pain as an indicator of tissue health and conclude that activity may further damage their tissue, decreased physical movements may be seen as a logical protective mechanism.[69] The results of this study would indicate that with decreased pain perception and a greater understanding of the nonmechanical factors that may increase or decrease nerve sensitivity (ie, failed treatment, fear, emotions, and different explanations of their pain), patients may be inclined to see themselves as less disabled and more inclined to increase their activity.[70-73]

Persistent pain has been shown to lead not only to significant physical changes in the brain,[22,74,75] but also to altered processing of pain and the activation of catastrophization.[76,77] With persistent pain, failed treatment, and different explanations for their pain, patients with chronic pain may plausibly view their condition as being far worse than it actually is and their future as bleak, and thus have little hope.[78-80] This irrational thought that patients have in believing their problems as being far worse than they actually are is known as catastrophization, and it appears to enhance pain processing. This review included patients with more than 2.5 years of chronic pain, which concurs with studies associating persistent pain with higher levels of catastrophization.[76,77,81] The deemphasis of the faulty tissue model as portrayed by the NE could be seen as 1 reason for its ability to begin to alter pain catastrophization.

Finally, we should consider a particular circumstance that is relevant to patients with MSK pain and how NE may facilitate therapeutic improvement. The nature of MSK pain is unique given its subjectivity, frequent lack of an "objective" radiographic correlate, and the many erroneous and often misleading things patients are told. These factors could trigger the development of maladaptive cognitions that, without adequate education during prior medical workups, reinforce fears of movement and the perception of serious tissue damage underpinning

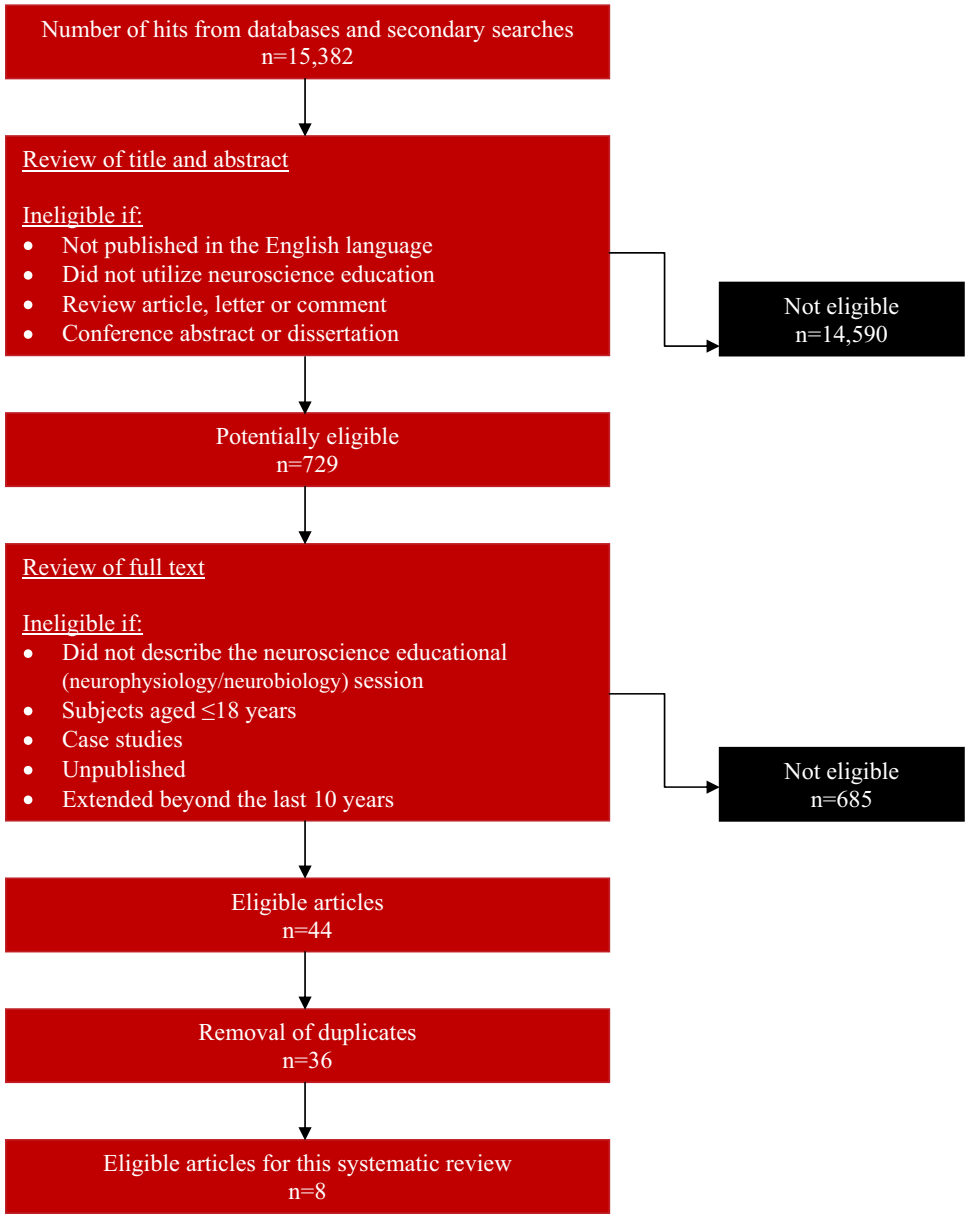

Fig 1. Retrieval and review process.

patients' pain (eg, "you have a bulging disk"; "you have degenerative joint disease"; "your nerve is being pinched"). NE may have potential impact by countermanding any iatrogenically induced maladaptive beliefs encouraged by treatment with physicians who practice pain management from the "tissue damage" perspective. These maladaptive beliefs are also often reinforced by misdirected and failed surgery or interventional procedures. Given the evidence for the importance of exercise in the management of MSK pain, these fears become primary in understanding continued disability and may help to explain why NE may be particularly well suited to interventions for MSK disorders.

Limitations

This systematic review has limitations that need to be acknowledged. The review is limited by the number of studies, as well as the need to use studies of lower levels of evidence to gain a better understanding of the effect of NE in MSK pain. The heterogeneous nature of studies in this review precluded true meta-analyses, which would have been helpful to determine the level of NE effectiveness. Based on the lack of consistent control groups in the articles reviewed, it is not possible to draw strong conclusions about the influence of the NE content versus individual attention and the acknowledgment that perceived pain may be real. This review contains mainly patients with CLBP and carryover of the results to other MSK conditions is limited. Additional limitations include English-only studies and patient populations, as well as excluding younger patients.

CONCLUSIONS

The results of this systematic review show compelling evidence for NE affecting passive[14,23,41] and active physical movements.[14,23,41] Positive effects of NE on pain perception, disability, and catastrophization may allow patients to apply this new view of their pain state by reappraising their ability to

move.[23] With the decreased threat of additional tissue injury and a newly gained realization that pain may be caused by neural sensitivity rather than tissue injury, patients may be able to actively move further and allow clinicians to passively move them further.

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